

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

LISTING OF CLAIMS

1. (Currently amended) A transgenic mouse having a genome that comprises a mutation of an endogenous *Npas3* gene, wherein the *Npas3* mutation causes a disruption that inactivates the gene, and a homozygous transgenic *Npas3* mutant mouse does not produce a fully functional NPAS3 protein, wherein the transgenic mouse exhibits a phenotype that models schizophrenia.
2. (Currently amended) The transgenic mouse of claim 1 wherein the disruption of the endogenous *Npas3* gene comprises a deletion of at least one exon of the *Npas3* gene, replaced with heterologous DNA sequence, ~~wherein the heterologous DNA sequence, preferably, comprises a gene expression cassette that confers antibiotic resistance to a host organism.~~
3. (Currently amended) The transgenic mouse of claim 1 wherein the disruption comprises a conditional disruption that is regulated by an inducible factor, ~~preferably selected from the group consisting of Cre recombinase in a Cre-lox system, Flpase in a FRT-Flpase system, and combinations thereof.~~
4. (Currently amended) The transgenic mouse of claim 1 wherein the ~~mouse exhibits a~~ exhibited phenotype is selected from the group consisting of dyskinesia of hindlimb and foot-clasping posture, parkinsonian gait of stride length and footprint pattern, altered neurotransmitter signaling selected from the group of neurotransmitter consisting of dopamine, serotonin, GABA, and glutamate[[:]], altered neurotransmitter signaling pathway selected from the group consisting of dopamine and serotonin; altered responses to glutamateric signaling pathways such that administration of a glutamate analog induces hyperstereotypic behavior[[:]], and combinations thereof.
- [[4.]] 5. (Currently amended) At least one cell derived from the transgenic mouse of claim 1 ~~wherein the cell is, preferably, a neuron and is preferably isolated from a brain region~~

~~selected from the group consisting of substantia nigra, striatum, hippocampus, anterior cingulate cortex, and prefrontal cortex.~~

[[5.]] 6. (Currently amended) A method for determining the effectiveness of a biologically active agent in a transgenic mouse, comprising the steps of:

- a. disrupting the at least one allele of an endogenous *Npas3* gene in the transgenic mouse wherein the disruption inactivates the gene,
- b. administering to the mouse the biologically active agent, and
- c. assessing for a change in a phenotype of the mouse, wherein the phenotype is a phenotype selected from the group consisting of dyskinesia of hindlimb and foot-clasping posture, parkinsonian stride length and pattern, impaired balance and motor coordination on a narrow beam, impaired locomotor activity, hypersterotypic behavior, impaired prepulse inhibition, impaired zero maze behavior, altered gene expression, altered protein synthesis, altered receptor activity, elevation of cAMP level, altered protein dephosphorylation and altered protein phosphorylation, and combinations thereof.

Claims 6 – 8 (canceled)

[[9.]] 10. (Currently amended) A method for determining the effectiveness of a biologically active agent in a cell line derived from a transgenic mouse, comprising the steps of:

- a. disrupting at least one allele of an endogenous *Npas3* gene in the transgenic mouse wherein the disruption inactivates the gene,
- b. isolating at least one cell from the transgenic mouse,
- c. deriving an immortalized cell line from the isolated cell,
- d. amplifying cells of the cell line,
- e. administering at least one biologically active agent to the cells of the cell line, and
- f. detecting a biochemical change in the cells of the cell line.

[[10.]] 11. (Currently amended) The method according to claim [[9]] 10 wherein the isolated cell is a neuron, ~~preferably~~ isolated from a brain region selected from the group consisting substantia nigra, striatum, hippocampus, anterior cingulate cortex, and prefrontal cortex.

[[11.]]12. (Currently amended) The method according to claim [[10]] 11 wherein the biochemical change is selected from the group consisting of changes in synthesis of dopamine or dopamine metabolites, gene expression, protein synthesis, receptor activity, elevation of cAMP level, protein dephosphorylation and protein phosphorylation, and combinations thereof.

[[12.]]13. (Currently amended) The method according to claim [[10]] 11 wherein the amplified cells of the cell line are placed in at least one multi-well culture plate for high-throughput screening of a number of biologically active agents.

14. (New) The transgenic mouse of Claim 1, wherein the transgenic mouse exhibits a phenotype that models schizophrenia with a mutation only of the endogenous *Npas3* gene.

15. (New) The transgenic mouse of Claim 2, wherein the heterologous DNA sequence comprises a gene expression cassette that confers antibiotic resistance to a host organism.

16. (New) The transgenic mouse of Claim 3 wherein the inducible factor selected from the group consisting of Cre-recombinase in a Cre-lox system, Flpase in a FRT-Flpase system, and combinations thereof.

17. (New) The transgenic mouse of Claim 5 wherein the cell is a neuron isolated from a brain region selected from the group consisting of substantia nigra, striatum, hippocampus, anterior cingulate cortex, and prefrontal cortex.